

REMARKS

Claims 14-27 have been canceled without prejudice or disclaimer. Claims 28-49 have been added and therefore are pending in the present application. Claims 28-49 are supported by claims 14-27. Claims 29-32 are further supported by page 7, lines 10-22 of the specification. Claim 33 is further supported by page 10, lines 8-12 of the specification.

The specification has been amended to delete all references to the protease derived from *Aspergillus sp.* CBS 102448. After the filing of the instant application, it was discovered that the results presented in the specification for this protease were not correct due to an impurity contained in the protease sample. Applicants will submit new figures 4-5 removing any reference to the protease derived from *Aspergillus sp.* CBS 102448.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Rejection of Claims 14 and 15 under 35 U.S.C. 102

Claims 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Hiller (U.S. Patent No. 4,239,750), Hiller (U.S. Patent No. 4,225,584), Hiller (U.S. Patent No. 4,218,437), or Lehmann et al. (U.S. Patent No. 4,062,732). This rejection is respectfully traversed.

The Hiller and Lehmann patents disclose animal feeds comprising an antibiotic and a protease. The protease can be produced from *Bacillus licheniformis*, *Bacillus natta*, and *Bacillus subtilis*. Furthermore, preferred proteases are acid proteases, e.g., from *Aspergillus niger* or those described in U.S. Patent Nos. 3,674,644 and 3,677,898. Particularly preferred proteases are from the genus *Trametes*, or from *Rhizopus rhizopodiformis* (described by Lehmann in U.S. Patent No. 4,062,732).

However, one of ordinary skill in the art would know that only some proteases from *Bacillus licheniformis*, *Bacillus natta*, and *Bacillus subtilis* are subtilisins and acid-stable. Other proteases from these organisms are either subtilisins or acid-stable and others are neither subtilisins nor acid-stable. Thus, this disclosure in the Hiller and Lehmann patents is not a disclosure of the use of a protease which is both acid-stable and a subtilisin derived from *Bacillus licheniformis*, *Bacillus natta*, and *Bacillus subtilis* in animal feed.

With respect to the other proteases disclosed in the Hiller and Lehmann patents, i.e., the *Rhizopus rhizopodiformis* CBS 227.75 protease, the *Aspergillus niger* protease and the *Penicillium*

and *Rhodotorula* proteases described in U.S. Patent Nos. 3,674,644 and 3,677,898, neither is a subtilisin.

Thus, the Hiller and Lehmann patents do not disclose an animal feed additive comprising a protease which is both a subtilisin and acid-stable, as claimed herein.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. The Rejection of Claims 14-16 under 35 U.S.C. 103

Claims 14-16 are rejected under 35 U.S.C. 103 as being unpatentable over Hiller (U.S. Patent No. 4,239,750), Hiller (U.S. Patent No. 4,225,584), Hiller (U.S. Patent No. 4,218,437) or Lehmann et al. (U.S. Patent No. 4,062,732) in view of Outtrup et al. (U.S. Patent No. 5,597,720). This rejection is respectfully traversed.

The Hiller and Lehmann patents are discussed in Section I. As noted above, neither patent discloses the use of an acid-stable subtilisin in animal feed.

Furthermore, of these four patents, the only patent to test the use of a protease alone in animal feed is U.S. Patent No. 4,218,437 (Hiller). In particular, Hiller states at column 5, lines 36-46:

The above two examples demonstrate that the addition of the antibiotic Virginiamycin at a level of either 7.5 ppm or 15 ppm slightly improves both the end weight and the feed utilization, whereas the addition of the acid proteases at a level of 0.45 mTU/gm scarcely effects the end weight or feed utilization. Completely unexpectedly, a combination of both causes an effect which is more than additive (emphasis added)....

Thus, the Office is incorrect at page 4 that the patents "demonstrate no particular advantage of one acid protease over another." In fact, the cited patents do not disclose any advantage of using a protease in animal feed.

The Office also contends that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute one acid protease for another in an animal feed additive, in particular the acid protease of Outtrup et al...." This is respectfully traversed.

Outtrup et al. disclose a protease preparation comprising PD498 from *Bacillus* sp., NCIMB 40484. The preparations disclosed in Outtrup et al. comprise the protease as well as Na (column 3/66), P (column 4/34), alkali metal salts (5/22), and various other components (column 5).

However, Outtrup et al. do not disclose animal feed additives and compositions, comprising an acid-stable protease, a vitamin and a trace mineral, as claimed herein.

Moreover, as stated above, the Hiller and Lehmann patents do not suggest there is any advantage to using a protease in animal feed in the absence of an antibiotic. Thus, one of ordinary skill in the art would not have been motivated to substitute another acid-stable protease for the proteases disclosed in the Hiller and Lehmann patents.

Moreover, the instant specification demonstrates that the use of proteases which are both subtilisins and acid-stable in animal feed result in significantly improved weight gain and feed conversion. In particular, Example 4 of the instant application describes an *in vitro* testing of a protease of the invention (the protease derived from *Bacillus* sp. NCIMB 40484) and four subtilisins which are not acid-stable (ALCALASE™, subtilisin Novo, subtilisin Novo (Y217L), and SAVINASE™). The results show that the protease of the invention has a significantly better effect on protein solubilization than the other proteases. Furthermore, Example 10 of the instant application describes an *in vivo* trial of the protease derived from *Bacillus* sp. NCIMB 40484. The results show that the use of the protease of the present invention resulted in a statistically significant improvement of feed conversion. Since these results could not have been predicted from the prior art, the results are surprising and unexpected.


For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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